B7-1 Therapeutic Cancer Vaccine for Metastatic Melanoma and Metastatic Breast Cancer

Technical Abstract

Despite considerable advances in elucidating the molecular basis of cancer and in the development of improved treatments, there has been no overall reduction in cancer mortality for the majority of patients with metastatic disease. For patients with metastatic melanoma, no treatments to date have had any impact on overall survival with a median survival of only 8-9 months. For women with metastatic breast cancer, chemotherapy and hormonal therapy offer a chance for palliation of symptoms but almost no opportunity for cure. New approaches to the treatment of metastatic breast cancer and metastatic melanoma are clearly needed. Strategies that use the immune system to target tumor cells are attractive. Recent advances in our understanding of how the cellular immune systems operates and the prerequisites of antigen recognition by T cells permit the design of novel immunotherapeutic approaches based on a more complete understanding of the system being manipulated.

The rationale for this human trial is based upon extensive preclinical studies that demonstrate in murine models that transduction of tumor cells with the B7 cDNA enhances the immunogenicity of the engineered tumor cells and that mice exposed to B7+ tumor cells can reject the B7- parental tumor cells.

The goals of this phase I study are to evaluate the safety and feasibility of treating patients with metastatic breast cancer and metastatic melanoma by intratumoral injections of an adenovirus vector containing the human B7-1 gene. Patients with incurable, advanced cancer who have accessible tumors (cutaneous, subcutaneous or lymph node) will be treated with intratumoral injections of H5.030CMVhB7. The overall objective of this study is to assess the local and systemic toxicity (the maximally tolerated dose) associated with the in vivo B7-1 gene transduction. Correlative laboratory studies will be conducted which will assess the immunologic effects of treatment with H5.030CMVhB7 as well as the success and duration of gene transfer.

In this study three dose levels will be tested. The starting dose was chosen for its apparent safety in preclinical animal studies. At least 2 tumor sites will injected. Four patients will be treated at each dose level. Patients will be monitored closely for side effects related to therapy. Sequential tumor biopsies of treated and untreated sites will be performed to access efficacy of gene transfer and immunological effects. Response to treatment will be assessed post therapy.